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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,337	BENOIT ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,7,9,11,14,15,17,19,21,23,25,27,29,31,33-37 and 39-56* is/are pending in the application.

4a) Of the above claim(s) *34-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed September 30, 2005.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33-37, and 39-56 are pending in the instant application. Claim 4 has been amended. Claims 34-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made with traverse in the reply filed on October 20, 2003.

It is noted that in the previous Office Action mailed June 1, 2005, claims 40-56 were indicated as being withdrawn since it was the Examiner's opinion that claims 40-56 were directed to an invention that is independent or distinct from the invention as originally claimed. In response, Applicant's argue that claims 40-56 are not drawn to a non-elected invention since the original claims recited the term "comprising" which includes SEQ ID NO:1 and fragments comprising SEQ ID NO:1. The Examiner agrees with Applicant's argument. Specifically, the Examiner agrees that since the original claims recited the term "comprising", this includes the full length of SEQ ID NO:1, in addition to fragments of SEQ ID NO:1. Therefore, claims 40-56 have been examined with the elected invention.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39-56 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

In the previous Office Action mailed June 1, 2005, claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed June 1, 2005. It is noted that claims 40-56 are also included in this rejection.

Response to Arguments

In response to this rejection, Applicants argue that the term "fragment" has been removed from claim 4 and therefore the instant rejection is obviated. This argument has not been found persuasive. Although the term "fragment" has been removed, claim 4 has been amended to recite "a polynucleotide comprising SEQ ID NO:2 **or a sequence having at least 80% sequence identity to SEQ ID NO:2**". The issue is that the specification as filed fails to adequately describe a polynucleotide sequence having at least 80% sequence identity to SEQ ID NO:2 which retains the function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed. It is noted that this functional limitation itself is not sufficient to provide a structure/function relationship for meeting the written description requirement because it is not clear what structure the polynucleotide sequence having at least 80% sequence identity to SEQ ID NO:2 would have by the recitation of the functionality alone, "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide". The specification provides no guidance

in this regard. Therefore, in the absence of any teaching by way of structure or reference to active domains or regions, one of skill in the art could not immediately envision a polynucleotide sequence having at least 80% sequence identity to SEQ ID NO:2, which retains the function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed.

In summary, only a polynucleotide comprising SEQ ID NO:2, but not a polynucleotide sequence having at least 80% sequence identity to SEQ ID NO:2, meets the written description provision of 35 U.S.C. 112, first paragraph.

Regarding claims 40-56, these claims recite "a polynucleotide comprising SEQ ID NO:1 **or a sequence having at least 93% sequence identity to SEQ ID NO:1**, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide". The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the

'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invention what is claimed." (See Vas-Cath at page 1116).

The specification provides adequate written description for a polynucleotide comprising SEQ ID NO:1, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide (see Example 10). However, the claims are so broad to include a polynucleotide sequence having at least 93% sequence identity to SEQ ID NO:1, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. The specification as filed fails to adequately describe a polynucleotide sequence having at least 93% sequence identity to SEQ ID NO:1 which retains the function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed. This functional limitation itself is not sufficient to provide a structure/function relationship for meeting the written description requirement because it is not clear what structure the polynucleotide sequence having at least 93% sequence identity to SEQ ID NO:1 would have by the recitation of the functionality alone, "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide". The specification provides no guidance in this regard. Therefore, in the absence of any teaching by way of structure or reference to active domains or

regions, one of skill in the art could not immediately envision those polynucleotide sequences having at least 93% sequence identity to SEQ ID NO:1, which retains the function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed.

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff vs. Electronics, Inc.*, 48 USPQ2d, 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In summary, only a polynucleotide comprising SEQ ID NO:1, but not a polynucleotide sequence having at least 93% sequence identity to SEQ ID NO:1, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

In the previous Office Action mailed June 1, 2005, claims 4, 5, 21, 23, 27, 31, 33, and 39 were rejected under 35 U.S.C. 102(b) as being anticipated by Kuo et al. (Development, 1999 Vol. 126:4223-4234). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed June 1, 2005. It is noted that this rejection is also applied to claims 40, 41, 49, 50, 52, and 54-56.

Response to Arguments

In response to this rejection, Applicants argue that the term "fragment" has been removed from claim 4 and therefore the instant rejection is obviated. This argument has not been found persuasive. Although the term "fragment" has been removed, claim 4 has been amended to recite "a polynucleotide comprising SEQ ID NO:2 or a sequence having at least 80% sequence identity to SEQ ID NO:2". In Applicant's response filed February 28, 2005, Applicants provided an alignment/BLAST sequence comparison of SEQ ID NO:2 with the p0.295Luc construct disclosed by Kuo et al. (see Exhibit B). It is noted that this construct shares 83% sequence identity to SEQ ID NO:2 (see Applicant's Exhibit B). In fact, Exhibit B is also replete with several sequences having *at least* 80% sequence identity to SEQ ID NO:2 as instantly claimed. For example, compare Applicant's Exhibit B Query[1] sequence at nucleobases -207 to -184 and -137 to -102 with Sbjct[2] nucleobases 1803 to 1826 and 1882 to 1918, respectively. These sequences have 100% sequence identity to SEQ ID NO:2. In this regard, the p0.295Luc construct disclosed by Kuo et al. is clearly a sequence having at least 80%

sequence identity to SEQ ID NO:2, and thus anticipates the instant invention.

The Examiner would like to point out that Kuo et al. disclose, regarding construct p0.295luc, "expression of the transgene was specific to both the myocardium of the heart and the somites, and cardiac expression was first detected at around E9.95. Cardiac expression of the transgene was restricted to the conotruncal and right ventricular segments of the primitive heart" (see page 4227, first column, last paragraph, and Figures 4D, H, and 5C). Therefore, construct p0.295luc clearly induces expression in cardiac cells *in vivo* as recited in claims 4, 5, 21, 23, 27, 31, 33, and 39.

Regarding claims 40, 41, 49, 50, 52, and 54-56, these claims recite "a polynucleotide comprising SEQ ID NO:1 or a sequence having at least 93% sequence identity to SEQ ID NO:1, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide". Kuo et al. disclose the sequence of a 2.5 kb fragment upstream of the coding sequence of the mouse CARP gene. It is noted that SEQ ID NO:1 of the instant invention consists of a portion of the sequence between -2266 and +92, relative to the transcription start position +1 of the mouse CARP gene. It is further noted that the p2.5Luc construct disclosed by Kuo et al. consists of a portion of the sequence between -2500 and +47, relative to the transcription start position +1 of the mouse CARP gene (see Figure 3). Therefore, SEQ ID NO:1 of the instant invention shares 100% sequence identity with the p2.5Luc construct disclosed by Kuo et al. at -2266 and +47 of the mouse CARP gene.

The Examiner would like to point out that Kuo et al. disclose, regarding construct the p2.5Luc, "expression of the transgene... was detected as early as around embryonic day (E) 8 in the cardiac crescent." "In neonates... cardiac expression of the transgene was restricted to both atria and the right ventricle" (see page 4227, first column). Therefore, construct p2.5Luc clearly induces expression in cardiac cells *in vivo* as recited in claims 40, 41, 49, 50, 52, and 54-56.

Therefore, Kuo et al. anticipate claims 40, 41, 49, 50, 52, and 54-56.

After careful reconsideration of the claims, a new grounds of rejection(s) is presented as detailed below:

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39-56 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39-56, recite the term "polynucleotide". The instant specification does not define the term "polynucleotide", however page 5, [014] recites "the invention relates to any polynucleotide of natural origin". The instant specification at page 5 [015] further recites, "polynucleotide of natural origin" is understood to mean a genomic DNA

fragment". Given this disclosure, the term "polynucleotide" recited in the claims reads upon a naturally occurring polynucleotide, which is a product of nature that does not clearly show the "hand of man". Language at the beginning of these claims such as "an isolated polynucleotide" would remove the instant rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Aihara, Y., GenBank Accession No. AF131884.

Claim 4 is drawn to a polynucleotide comprising SEQ ID NO:2 or a sequence having at least 80% sequence identity to SEQ ID NO:2, wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide.

Aihara disclose GenBank Accession No. AF131884, which is a 2074 bp fragment of the human CARP gene. It is noted that GenBank Accession No. AF131884 is 100% identical to SEQ ID NO:2 of the instant invention.

The burden of establishing whether the prior art human CARP gene fragment has the further function of specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said fragment under generally any assay conditions as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that prior art human CARP gene fragment disclosed by Aihara would or would not have the additional functional limitation of "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said fragment" under generally any assay conditions.

Therefore, absent evidence to the contrary, claim 4 is anticipated by Aihara, Y.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
December 15, 2005